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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/642,492
Filing Date	August 18, 2000
First Named Inventor	Gary VAN NEST
Art Unit	1648
Examiner Name	E. Le
Total Number of Pages in This Submission: 11	Attorney Docket Number: 377882000800

ENCLOSURES (*Check all that apply*)

- [ ] Fee Transmittal Form
- [ ] Fee Attached
- [ ] Amendment/Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
- [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
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- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) (please Identify below):
  - Communication in Response to Notification of Non-Compliant Appeal Brief (10 pages)
  - Return Receipt Postcard

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	MORRISON & FOERSTER LLP (Customer No.: 25226)		
Signature	Jill A. Jacobson		
Printed name	Jill A. Jacobson		
Date	December 28, 2006	Reg. No.	40,030

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EV534442434US, on the date shown below in an envelope addressed to: MS Appeal Brief - Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: December 28, 2006 Signature: _____ (Lori Sims)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EV534442434US, on the date shown below in an envelope addressed to: MS Appeal Brief - Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: December 28, 2006 Signature: (Lori Sims)

Docket No.: 377882000800
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Gary VAN NEST et al.

Application No.: 09/642,492 Confirmation No.: 7136

Filed: August 18, 2000 Art Unit: 1648

For: METHODS OF MODULATING AN IMMUNE RESPONSE USING IMMUNOSTIMULATORY SEQUENCES AND COMPOSITIONS FOR USE THEREIN Examiner: E. Le

COMMUNICATION IN RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is in response to the Notification of Non-Compliant Appeal Brief mailed on December 5, 2006, for which a response is due on January 5, 2007. This response is timely filed.

REMARKS

The Notification states that the brief "does not show which independent claim(s) belongs to which page and line number of the specification and drawings if any." Applicants' representative spoke with Mr. Everett R. Williams, Patent Appeals Specialist, whose name appears at the bottom of the Notification of Non-Compliant Appeal Brief, on December 21, 2006. Mr. Williams advised Applicants' representative that the brief should be re-filed, with a paragraph added below each independent claim recited in the section entitled "V. Summary of Claimed Subject Matter," identifying the page and line numbers of support for the particular independent claim which each such paragraph follows.

Applicants disagree that the Appeal Brief as filed on July 12, 2006, and as re-filed on November 6, 2006 in response to the first Notification of Non-Compliant Appeal Brief mailed October 18, 2006, is non-compliant with 37 C.F.R. §41.37. Applicants note that the text of 37 C.F.R. §41.37(c)(1)(v) states that the summary of claimed subject matter must contain "[a] concise explanation of the subject matter defined in each of the independent claims involved in the appeal, which shall refer to the specification by page and line number, and to the drawing, if any, by reference characters." Applicants provided such a concise explanation in the subsection entitled "Support and significance of claim terms," which immediately follows the recitation of independent claims involved in the appeal. The subsection describes in detail the support for each limitation of the independent claims on appeal, referring to such support by page and line number, and referring to the limitations in the independent claims which were designated by underlined text. Thus, in the Appeal Brief as filed, Applicants provided a concise explanation of the subject matter defined by each independent claim on appeal, referring to the specification by page and line number, as required by 37 C.F.R. §41.37. Applicants respectfully submit that the Appeal Brief as filed was compliant and that the issuance of the Notification of Non-Compliant Appeal Brief was improper.

However, solely in the interest of expediency and without agreement that the Appeal Brief as filed is non-compliant, Applicants are filing an amended version of Section V herewith. Section V of the brief has been amended to include a statement following each independent claim

setting forth the support for that claim in the specification by page and line number. In accordance with MPEP §1205.03, Applicants are re-filing only Section V of the Appeal Brief, and are not re-filing the entire brief. The MPEP states that "[w]hen the Office holds the brief to be defective solely due to appellant's failure to provide a summary of the claimed subject matter as required by 37 CFR 41.37(c)(1)(v), *an entire new brief need not, and should not, be filed. Rather, a paper providing a summary of the claimed subject matter as required by 37 CFR 41.37(c)(1) will suffice.*" MPEP §1205.03, emphasis added. Accordingly, Applicants are filing only Section V as amended, attached herewith below, rather than the entire Appeal Brief. In a telephone conference on December 27, 2006, Mr. Everett R. Williams confirmed to Applicants' representative that this procedure would provide an appropriate response to the pending Notification of Non-Compliant Appeal Brief.

AMENDMENT OF APPEAL BRIEF

Please replace Section V of the Appeal Brief with the following amended section:

--V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is based on the discovery that modulation of an immune response to an antigen (a "second antigen") may be achieved by co-administration of the antigen and another antigen (a "first antigen") that is covalently conjugated to an immunomodulatory polynucleotide that contains an immunostimulatory sequence ("ISS"). Administration of the immunomodulatory polynucleotide-first antigen conjugate elicits an immune response, particularly a Th1 response, to the second antigen.

ISS polynucleotides were well known in the art prior to filing of this application, as well as how to make them and how to identify and test such sequences for immunostimulatory activity. It was also known in the art that conjugation of an antigen to an ISS will stimulate an immune response. However, it was not known until the present invention by Applicants that administration of an ISS-antigen conjugate could stimulate an immune response to a second, unconjugated antigen. The inventors have discovered that administration of an ISS-containing polynucleotide–first antigen conjugate advantageously permits immune modulation at a significantly lower dose and with a stronger interferon gamma response and an enhanced CTL response with respect to the second antigen, as compared to administration of second antigen alone.

The benefit of this novel approach is that it alleviates the need to design and manufacture different formulations for each antigen against which generation of an immune response would be desirable. For example, in the context of immunization against a pathogen, rapid mutation in some antigenic proteins, such as coat proteins, would not necessitate characterization of the changes and reformulation of a vaccine to reflect those changes, because administration of an immunomodulatory polynucleotide-first antigen conjugate enables immunization against antigenic determinants of the co-administered pathogen regardless of the polypeptide sequences of the antigenic portions.

Claims under consideration

There are three independent claims under consideration in the application on appeal, claims 1, 37, and 40.

Claim 1

Claim 1 is directed to a method of modulating an immune response to a second antigen in an individual comprising co-administering (i) a complex comprising an immunomodulatory polynucleotide covalently conjugated to a first antigen, and (ii) a second antigen, at the same site in the individual and in an amount sufficient to modulate an immune response in the individual to the second antigen, wherein the polynucleotide comprises an immunostimulatory sequence ("ISS") comprising the sequence 5'-cytosine, guanine-3'.

Claim 1 is supported in the specification on page 6, lines 8-31; page 9, line 17 – page 10, line 32; page 13, lines 1-15; page 15, lines 19-23; and page 16, line 13 – page 17, line 26.

Dependent claims add limitations that further specify the nature of the first antigen, further specify that the immune response is modulated by stimulating a Th1 response to second antigen and specify stimulation of production of specific molecules associated with the immune response, further specify sequence requirements for the ISS, or further specify that the individual is a mammal, such as a human.

Claim 37

Claim 37 is directed to a composition comprising (i) a complex comprising an immunomodulatory polynucleotide covalently conjugated to a first antigen, and (ii) a second antigen, wherein the polynucleotide comprises an ISS comprising the sequence 5'-cytosine, guanine-3', and wherein the first antigen is a viral conserved polypeptide and the second antigen is a viral variable polypeptide.

Claim 37 is supported in the specification on page 9, line 17 – page 10, line 32; page 11, lines 13-31; page 16, line 13 – page 17, line 26; and page 49, lines 12-20.

Dependent claims add limitations that further specify the nature of the first antigen.

Claim 40

Claim 40 is directed to a composition comprising (i) a complex comprising an immunomodulatory polynucleotide covalently conjugated to a first antigen, and (ii) a second antigen, wherein the polynucleotide comprises an ISS comprising the sequence 5'-cytosine, guanine-3', and wherein the first antigen is an allergen .

Claim 40 is supported in the specification on page 9, line 17 – page 10, line 32; page 12, lines 21-27; page 16, line 13 – page 17, line 26; and page 49, lines 12-14.

Dependent claims add limitations that further specify the nature of the first antigen.

Support and significance of claim terms

The support in the specification and significance of each of the features recited in the independent claims is discussed below:

Modulating an immune response "Modulating an immune response" refers to immunostimulatory and immunosuppressive effects, as described on page 9, line 31 – page 10, line 15.

Individual The term "individual" refers to a vertebrate, preferably a mammal, such as a human, as described on page 13, lines 1-3 of the specification.

Co-administering The term "co-administering" refers to the administration of at least two different substances, *i.e.*, an immunomodulatory polynucleotide-first antigen complex and a

second antigen, sufficiently close in time to modulate an immune response, as described on page 13, lines 12-15.

Complex The term "complex" in the context of a conjugate as claimed, refers to a linked ISS-containing polynucleotide and antigen, as described on page 10, lines 16-18.

Immunomodulatory polynucleotide An "immunomodulatory" polynucleotide refers to a polynucleotide that mediates immunostimulatory or immunosuppressive effects, as described on page 9, line 31 – page 10, line 15. A "polynucleotide" or "oligonucleotide" is described on page 9, lines 25-30, as including single-stranded DNA (ssDNA), double-stranded DNA (dsDNA), single-stranded RNA (ssRNA) and double-stranded RNA (dsRNA), modified oligonucleotides and oligonucleosides or combinations thereof. The oligonucleotide can be linearly or circularly configured, or the oligonucleotide can contain both linear and circular segments. (The terms "polynucleotide" and "oligonucleotide" are used interchangeably in the specification.)

Covalently conjugated A covalent "conjugate" refers to a complex in which an ISS-containing polynucleotide and an antigen, *i.e.*, the "first antigen" in the claimed methods and compositions, are covalently linked, as described on page 10, lines 16-18.

First antigen The term "first antigen," *i.e.*, the antigen that is covalently conjugated to the immunomodulatory polynucleotide in the claimed methods and compositions, refers to a substance that is recognized and bound specifically by an antibody or by a T cell antigen receptor, as described on page 10, lines 19-26.

Second antigen The term "second antigen" refers to a different antigen than the first antigen, including a different antigenic region within the same polypeptide, which is administered to an individual, and against which an immune response is modulated by the methods of the invention, as described on page 10, lines 27-32.

At the same site The specification describes administration of the first antigen and immunomodulatory polynucleotide at the same site as the second antigen on page 15, lines 19-23. The specification states that "[f]or example, if the second antigen is encountered at the mucosa, such as lung or vaginal tissue, then the immunomodulatory polynucleotide and first antigen are

administered to the relevant mucosa." In the context of the claimed methods, in which the immunomodulatory polynucleotide-first antigen complex is co-administered with the second antigen at the same site, both components are administered to the same tissue site sufficiently close in time to modulate an immune response (see description of "co-administration" on page 13, line 12-15).

Amount sufficient to modulate an immune response A "sufficient amount" to modulate an immune response refers to the amount of the claimed immunomodulatory polynucleotide-first antigen complex that is sufficient to effect beneficial or desired results, *i.e.*, an amount sufficient to modulate an immune to a second antigen compared to the immune response obtained when the second antigen is administered alone, as described on page 13, lines 4-11.

Immunostimulatory sequence ("ISS") The terms "immunostimulatory sequence" and "ISS" refer to a polynucleotide sequence that effects a measurable immune response as measured *in vitro*, *in vivo*, and/or *ex vivo*, as described on page 9, lines 17-24.

Comprising the sequence 5'-cytosine, guanine-3' The ISS can be of any length greater than 6 bases or base pairs and generally comprises the sequence 5'-cytosine, guanine-3', as described on page 16, lines 11-12. Other embodiments of the ISS sequence are described on page 16, line 13 – page 17, line 26.

Viral conserved polypeptide A viral "conserved" polypeptide refers to a viral polypeptide (or a region or domain of a polypeptide) that does not mutate, or change its sequence, at an appreciable rate, for example, a constant domain that is not prone to vary between strains and/or species of virus, as described on page 11, lines 13-25.

Viral variable polypeptide A viral "variable" polypeptide refers to a viral polypeptide (or a region or domain of a polypeptide) that mutates at an appreciable rate, for example, some viral coat proteins, as described on page 11, lines 25-31.

Allergen The term "allergen" refers to an antigen or antigenic portion of a molecule, usually a protein, which elicits an allergic response upon exposure to a subject, as described on page

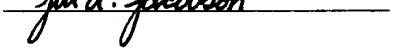
12, lines 21-27. Examples of a number of isolated allergens are provided in Table 1 on pages 22-25.--

CONCLUSION

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 377882000800. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 28, 2006

Respectfully submitted,

By 

Jill A. Jacobson
Registration No.: 40,030
MORRISON & FOERSTER LLP
755 Page Mill Road
Palo Alto, California 94304-1018
(650) 813-5876